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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/650,337	08/28/2000	William J. Dower	44368-0001 US C7	8260

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HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
01/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/650,337	DOWER ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2007 and 17 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *74-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *74-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12 July 2007 has been entered.

DETAILED ACTION

This Office Action is in response to the amendment filed 12 July 2007 and 17 October 2007. Claims 1-73 have been cancelled. Claims 74-76 are pending.

The objection to claim 75 for containing nucleotide sequences not appended with SEQ ID NO. is **withdrawn** in response to the amendment.

Double Patenting

The nonstatutory double patenting rejection of claims 74-76 as being unpatentable over claims 1, 39 and 40 of US Patent No. 5,723,286 is **withdrawn** in withdrawn in view of Applicants' arguments.

NEW REJECTION: Claims 74-76 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 39 and 40 of U.S. Patent No. 5,723,286. Although the conflicting claims are not identical, they are not patentably distinct from each other because the limitation in the patented claim 2,

"further comprising the step of sequencing a region of said expression vectors comprising said oligonucleotides of selected bacteriophage," would be obvious to identify the polynucleotide sequence that encodes a peptide which binds to a preselected receptor molecule. If the amino acid sequence of the selected peptide is known, one skilled in the art can readily ascertain the nucleotide sequence encoding it.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claim 74 under 35 U.S.C. §103(a) as being obvious over Kauffman *et al.* (US 5,723,323, effectively filed on 20 November 1986) in view of de la Cruz *et al.* (1988, No. BG in IDS) and Singekawa *et al.* (1988, No. CC in IDS) is **withdrawn** in view of Applicants' amendment.

NEW REJECTIONS - Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 74-76 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a method comprising transforming host cells with

filamentous phage expression vectors encoding a fusion protein comprising a hexapeptide fused to the N-terminus of a processed or mature pIII coat protein, does not reasonably provide enablement for (1) any other size peptide; (2) fusion with unprocessed coated protein; and (3) any other type of filamentous phage coat protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The limitation in claims 75 and 76 "comprising a peptide fused to a coat protein of a filamentous bacteriophage" is read as fusion to either the N-terminus or C-terminus of the coat protein but never as insertion between the coat protein.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors (MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and *Ex Parte Forman*, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The nature of the invention is phage display of foreign protein by fusion with the filamentous phage coat protein for presentation on the surface of the bacteriophage.

The breadth of the instant claims encompasses any filamentous phage coat protein, including the minor coat proteins, pIII, pVII, pIX, pVI, and the major coat protein pVIII, in both unprocessed and processed forms. The breadth of claims 75 and 76 encompasses both N-terminal and C-terminal fusion.

The disclosure provides one working example wherein a hexapeptide is fused to the N-terminus of the processed coat protein pIII. The guidance in the specification limits the coat protein to only pIII in the processed form as the specification states on page 23: Constructing a library of peptides displayed on the N-terminus of processed pIII necessarily alters amino acids in the vicinity of the signal peptidase cleavage site. Certain changes in the corresponding region of the major coat protein, pVIII, have been shown to reduce processing efficiency, slowing or preventing the incorporation of pVIII to virions. The specification further discloses on page 17 that the claimed fusion technology is also limited to processed coat protein because bacteriophage coat protein, pIII, is made as a preprotein with an 18 amino acid leader sequence that directs pIII to the inner membrane of the bacterial host cell before it becomes assembled into an intact phage particle (Goldsmith and Konigsberg). Accordingly, fusing a foreign peptide to the unprocessed pIII would interfere with the assembly of the phage particle and the display of the peptide on the surface of the phage particle.

The specification also discloses on page 17 that the signal peptidase site for cleaving the peptide of phage is located to the N-terminus of the mature pIII. Accordingly, fusing the foreign peptide to the C-terminus of the mature pIII, where no signal peptidase site is present, would prevent a skilled artisan to obtain the desired

peptide from the bacteriophage by enzyme cleavage. In conclusion, the specification provides guidance that limits the instant invention by fusion site (N-terminus) and the form and type of the coat protein (process pIII). Therefore, the guidance in the specification and the working example fail to provide sufficient embodiments to enable the full scope of the claimed invention.

At the time of the invention, the state of art only recognizes filamentous fusion phage display technique that entails insertion of foreign DNA fragments into filamentous phage gene III to create a fusion protein with the foreign sequence in the middle (Smith, 1985; Parmley and Smith, 1989; see IDS). Malik *et al.* teach a high level of unpredictability in the size of peptides displayed on the pVIII coat protein of filamentous bacteriophage (Malik, 1996). Ilyichev *et al.* teach that inserting foreign DNA fragments into filamentous phage coat protein pVIII may change the position of the processing site (Ilyichev, 1992). This high level of unpredictability regarding the size of the display peptide, the site of fusion, the type of filamentous phage coat protein combined with the limited guidance in the specification is Applicants' invitation to undue and unpredictable experimentation to further test all other coat proteins, different size peptides, and C-terminal fusion sites for fusion phage display.

Legal precedence dictates that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 21 (C.C.P.A. 1976). Thus, when all the aforementioned factors are considered *in toto*, it would

clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
21 December 2007

Louise Humphrey, Ph.D.
Assistant Examiner